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Poster presentation

Mechanisms of relaxant activity of BAY 41-2272 in rat tracheal smooth muscle *in vitro*

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Background

The soluble guanylyl cyclase (sGC) is expressed in airway smooth muscle, and agents that stimulate sGC activity cause airway smooth muscle relaxation and bronchodilation. BAY 41-2272 is a potent nitric oxide (NO)-independent sGC stimulator, but little is known about its effects in airway smooth muscle. Therefore, this study aimed to investigate the mechanisms underlying the relaxations of rat tracheal smooth muscle induced by BAY 41-2272.

Methods

Tracheal rings were mounted in 10-ml organ baths for isometric force recording. BAY 41-2272 (0.0001–100 μM) concentration-dependently relaxed carbachol-precontracted tracheal rings (pEC50 = 6.68 ± 0.14).

Results

The NO synthesis inhibitor L-NAME (100 μM) and the sGC inhibitor ODQ (10 μM) caused significant rightward shifts in the concentration-response curves to BAY 41-2272. In addition, BAY 41-2272 (0.01 and 0.1 μM) increased the cGMP levels (approximately 2.2- and 4.2-fold, respectively), and significantly potentiated the sodium nitroprusside-induced relaxations. At the higher concentrations (0.03–1 μM), BAY 41-2272 shifted to the right the tracheal contractile responses to either carbachol (0.001–10 μM) or electrical field stimulation (EFS, 1–32 Hz). BAY 41-2272 (1 and 10 μM) also caused a marked rightward shift and decreased the maximal contractile responses to extracellular $CaCl_2$.

Conclusion

Our results indicate that BAY 41-2272 potently relaxes the rat tracheal smooth muscle in a synergistic fashion with exogenous NO. BAY 41-2272, at higher concentrations, has an additional mechanism involving Ca^{2+} entry blockade.